In the Claims

Please replace all prior versions, and listings, of claims in the application with the following list of claims:

1-20. (Cancelled)

21. (Currently Amended) A method of determining the level of histone covalent modification in a biological sample comprising:

contacting a biological sample with a fusion protein reporter comprising a core comprising a histone-modification-specific binding domain conjugated to a histone polypeptide, wherein the core is flanked by donor and acceptor fluorescent moieties, and

monitoring the level of fluorescence resonance energy transfer (FRET) between the donor and acceptor fluorescent moieties as a result of contact with the biological sample,

wherein the level of FRET is a measure of the level of histone covalent modification in the biological sample, and

wherein the histone covalent modification is acetylation, methylation or phosphorylation.

22. (Original) The method of claim 21, wherein the biological sample is selected from the group consisting of cells and tissues.

23. (Original) The method of claim 22, wherein the biological sample is a cell.

24. (Original) The method of claim 23, wherein the cell is undergoing cell division.

25. (Original) The method of claim 21, wherein the histone-modification specific binding domain is conjugated to the histone polypeptide with a linker molecule.

26. (Previously Presented) The method of claim 21, wherein the fusion protein reporter, further comprises one or more additional histone-modification-specific binding domains.

27. (Original) The method of claim 21, wherein the histone polypeptide is selected from the group consisting of H3 and H4.

28. (Original) The method of claim 21, wherein the histone polypeptide is selected from the group consisting of the N-terminus of H3 and the N-terminus of H4.

29. (Previously Presented) The method of claim 21, wherein the donor fluorescent moiety is selected from the group consisting of cyan fluorescent protein (CFP), enhanced cyan fluorescent protein (ECFP), and A206K mutants thereof.

30. (Original) The method of claim 21, wherein the acceptor fluorescent moiety is selected from the group consisting of yellow fluorescent protein (YFP), enhanced yellow fluorescence protein (EYFP), Citrine, Venus, and A206K mutants thereof.

31. (Cancelled)

32. (Currently Amended) The method of claim 21, wherein the histone-modification-specific binding domain is selected from the group consisting of[[:]] 14-3-3, FHA, WW, bromodomain, and chromodomain.

33. (Withdrawn and Original) The method of claim 32, wherein the bromodomain comprises the amino acid sequence set forth as SEQ ID NO: 3.

34. (Currently Amended) The method of claim 32, wherein the bromodomain is selected from the group consisting of[[:]] Gcn5, $TAF_{II}250$, P/CAF, CBP, BRG1, Swi2, and Sth1.

35. (Currently Amended) The method of claim 32, wherein the chromodomain is selected from the group consisting of [[:]] HP1, MRG15, MRG-1, cynCDY, Hrp3, dMi-2, CHD5, Swi6, and pdd3p.

36. (Original) The method of claim 21, wherein the histone polypeptide is a polypeptide substrate for the histone-modification-specific binding domain.

37. (Withdrawn and Original) The method of claim 21, wherein the histone polypeptide is an H3 polypeptide comprising the amino acid sequence set forth as ARTKQTARKSTGGKAPRKQLATKAARKSAPATGGVKKPHR (SEQ ID NO:1).

38. (Currently Amended) The method of claim 21, ~~wherein,~~ wherein the histone polypeptide is an H3 polypeptide comprising the amino acid sequence set forth as ARTKQTARKSTGGKAPRKQLATKAARKSAP (SEQ ID NO:18).

39. (Withdrawn and Original) The method of claim 21, wherein the histone polypeptide is an H4 polypeptide comprising the amino acid sequence set forth as SGRGKGGKGLGKGGAKRHRKVLRDNIQGIT (SEQ ID NO:2).

40. (Original) The method of claim 21, wherein the fusion protein reporter further comprises a targeting polypeptide, associated with the fusion protein.

41. (Original) The method of claim 40, wherein the targeting polypeptide is selected from the group consisting of a receptor ligand and a nuclear localization sequence (NLS), nuclear export signal (NES), plasma membrane targeting signal, a histone binding protein, and a nuclear protein.

42. (Previously Presented) The method of claim 21, further comprising:

monitoring a subsequent second level of FRET in the biological sample, and comparing the first and second levels of FRET as a measure of the change in the level of histone covalent modification in the biological sample.

43. (Original) The method of claim 21, further comprising:

comparing the level of fluorescence resonance energy transfer (FRET) in the biological sample to a control level of FRET as a determination of a histone modification disorder in the biological sample.

44. (Original) The method of claim 43, wherein the biological sample is from a subject and the determination of a histone modification disorder in the biological sample is diagnostic for a histone modification disorder in the subject.

45. (Original) The method of claim 43, wherein the control level of FRET is the level of FRET in a biological sample free of a histone-modification disorder.

46-129. (Cancelled)

130. (Previously Presented) The method of claim 21, wherein the level of FRET is increased following contact with the biological sample.

131. (Previously Presented) The method of claim 21, wherein the level of FRET is decreased following contact with the biological sample.

132. (New) A method of determining the level of histone covalent modification in a biological sample comprising

contacting a biological sample with a fusion protein reporter comprising a core comprising a histone-modification-specific binding domain conjugated to a histone polypeptide, wherein the core is flanked by donor and acceptor fluorescent moieties, and

monitoring the level of fluorescence resonance energy transfer (FRET) between the donor and acceptor fluorescent moieties as a result of contact with the biological sample,

wherein the level of FRET is a measure of the level of histone covalent modification in the biological sample, the histone covalent modification is phosphorylation, and the histone-modification-specific binding domain is a 14-3-3, FHA or WW domain.

133. (New) A method of determining the level of histone covalent modification in a biological sample comprising

contacting a biological sample with a fusion protein reporter comprising a core comprising a histone-modification-specific binding domain conjugated to a histone polypeptide, wherein the core is flanked by donor and acceptor fluorescent moieties, and

monitoring the level of fluorescence resonance energy transfer (FRET) between the donor and acceptor fluorescent moieties as a result of contact with the biological sample,

wherein the level of FRET is a measure of the level of histone covalent modification in the biological sample, the histone covalent modification is acetylation, and the histone-modification-specific binding domain is a bromodomain.

134. (New) A method of determining the level of histone covalent modification in a biological sample comprising

contacting a biological sample with a fusion protein reporter comprising a core comprising a histone-modification-specific binding domain conjugated to a histone polypeptide, wherein the core is flanked by donor and acceptor fluorescent moieties, and

monitoring the level of fluorescence resonance energy transfer (FRET) between the donor and acceptor fluorescent moieties as a result of contact with the biological sample,

wherein the level of FRET is a measure of the level of histone covalent modification in the biological sample, the histone covalent modification is methylation, and the histone-modification-specific binding domain is a chromodomain.